

Connective Tissue Diseases

- diseases of
Dermis.

(1) Lupus erythematosus (LE)

(Zebra hamra)

Chronic discoid EL	Subacute cutaneous LE	A systemic LE	Mixed C.T diseases	Drug induced LE
<ul style="list-style-type: none"> • Skin lesions +ve. • Systemic lesions : -ve • Serology : -ve the ANA in few PT's • HLA B7 & B8 	<ul style="list-style-type: none"> • Skin lesions : + • Systemic lesions : + (muscle joint) • Serology : +ve Anti-Ro & Anti- La • HLA-DR3 & B8 	<ul style="list-style-type: none"> • Skin lesions : +ve • Systemic lesions : ++ve • Serology : +ve ANA +ve and <u>antismith</u> • No HLA -association 		<p>+ve antihistone = +ve</p>

[I] Chronic Cutaneous Lupus Erythematosus

(Discoid LE)

* Epidemiology :

- Age : 40-80 years old.
- Sex : female : male = 2 : 1 (more severe in blacks)
- ↑ incidence of HLAB7 & B8

* Clinically :

- precipitating factor
- PPF : infection, stress, sunburn & drugs e.g. griseofulvin.
 - N.B. : "It may start spontaneously"
 - Exacerbating factors : sunlight.
 - Symptoms : Disfiguring erythematous scaly lesions mostly in

the face.

* healing → thin, white, atrophic, non contractile scar

Causes of ulcer in DLG:-

- Ischaemic
- Systemic
- ulcerative type.

+ ANA → elderly
weak in DLG
pregnancy
malignancy

Types of scales in Derm

Myca scale → pityriasis Lichenoid Chronica

adherent " → DLG

Laminated → Ps

Cigarette paper → T. versicolor

Collarette → P. Rosea.

- Signs :

> Sites lesions usually affect the sun exposed areas i.e. :
Face (specially the cheeks & bridge of nose
{butterfly area} ears & V-shaped area of the chest.

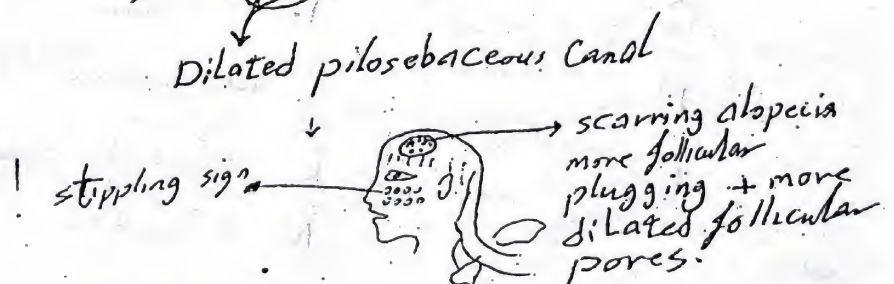
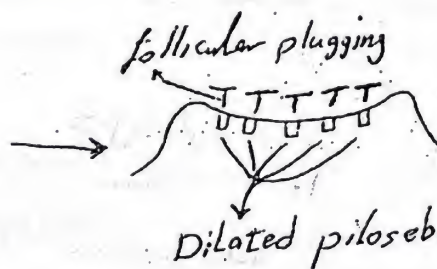
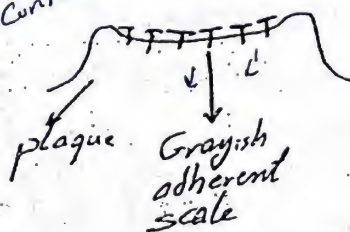
> Lesions are in the form of well defined erythematous plaques with variable shape & size having an elevated border. The border of the plaque adjacent to the skin is sometimes telangectatic.

> The surface of the plaques is covered with small grayish adherent scales which when removed, their under-surface show horny plug. This horny plug has occupied a dilated pilosebaceous canal (follicular plugging). The follicles become dilated & prominent giving what is called stippling sign. The center of the lesion is usually depressed.

> The lesions tend to heal with scarring, atrophy & pigmentary changes. (no treatment → skin cancer)

> On the scalp the plaques show more infiltration & more scar formation. Plugging & dilatation of the follicles are more pronounced. Loss of hair is permanent (cicatricial alopecia).

healed with
thin white non-atrophic
non-contractile
scar
D.O up & vulgus
contractile scar



Clinical variants

- ① Localized.
- ② generalized.
- ③ hypertrophic.
- ④ papular DLG → pruritic papule on the back → resulting in acneform hypertrophic follicular scar.
- ⑤ Roseacea like DLG → diffuse erythema reddish nodules (but not pustules) on cheeks, nose, forehead, chin.
- ⑥ palmo-planter erosive DLG.
- ⑦ annular atrophic DLG.
- ⑧ Telangiectatic DLG → persistent reticulate telangiectasia face / ear / neck / dorsa of hands.
- ⑨ LE gyratum repens:- migratory gyrate annular erythema + histological feature of DLG + underlying carcinoma
- ⑩ ~~Lupus profundus~~.

Other clinical types of DLG :- ① Classical.

DLG

ion... erythema, induration
 . heal without scarring
 . No scales
 . No follicular plugging.
 . Common on face
 . very low prevalence SLG

DLF → Non specific.

HLP → normal epi
 dermal inf. intake ē
 marked mucin deposition

Lupus panniculitis

intense inflammation of SC fat
 - Firm nodules or plaque sharply defined & normal overlying skin
 better felt than seen
 . healing with cup shaped depression.
 . Some patients have discoid lesion overlying the panniculitis
 Face, upper trunk, upper arm, Breast, Buttock, thigh

Chilblain lupus

. Red or dusky papule. papule or nodule.
 . on toes, fingers, nose, knee, elbow
 . DLG present elsewhere
 . Caused and exacerbated by cold or pregnancy.

G generalized

P $\left\{ \begin{array}{l} \text{papular} \\ \text{palmo-planter} \\ \text{profunda} \end{array} \right.$

L localized

H hypertrophic

T telangiectatic

L $\left\{ \begin{array}{l} \text{Lp over lap} \\ \text{syndrome} \\ \text{LE gyratum repens} \end{array} \right.$

R Roseacea like

pernio
 ① DLG
 ② sarcoidosis
 ③ perniosis

mucous membrane affection (3-7), nail affection, eye affection, ecthyma
Cong. redness

N.B. :

→ Active DLE lesions are bright red, while on healing lesions may show pink or white (hypomelanoatic) macules & scars. Lesions may show hyperpigmentation especially in persons with brown or black skin.

atrophic
non contractile

→ 5% of cases of DLE change into SLE.

→ Neoplastic changes e.g. SCC or BCC occur on top of DLE. They are often aggressive.

لupus

Clinical Types :

1- Localized DLE. Lesions are localized above the neck.

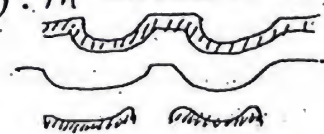
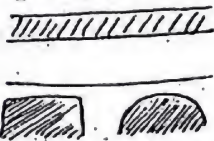
2- Generalized (Disseminated) DLE. Lesions are above & below the neck.

3- Hypertrophic (verruca DLE) :

- Non pruritic papulonodular lesions simulating hypertrophic LP or keratoacanthoma.

- Treatment : Intralesional steroid.

4- Lupus profundus (lupus panniculitis) : in subcutaneous tissue



• Firm S.C plaques or nodules with normal overlying skin.

• The nodules or plaque are better felt than seen.

→ Healing occur with cup-shaped depression (depressed scar)

لupus

atrophy → canker
hypopigmented or depigmented

5- LE-lichen planus overlap syndrome.

D.D. Causes of pigmentary incontinence, -

- ① LP ② LE
- ③ LSA ④ FDE
- ⑤ Dermatomyositis.
- ⑥ incontinent pigmenti

D.D. of Colloid bodies $\begin{matrix} \swarrow \text{LE} \\ \searrow \text{LP} \end{matrix}$

Colloid bodies

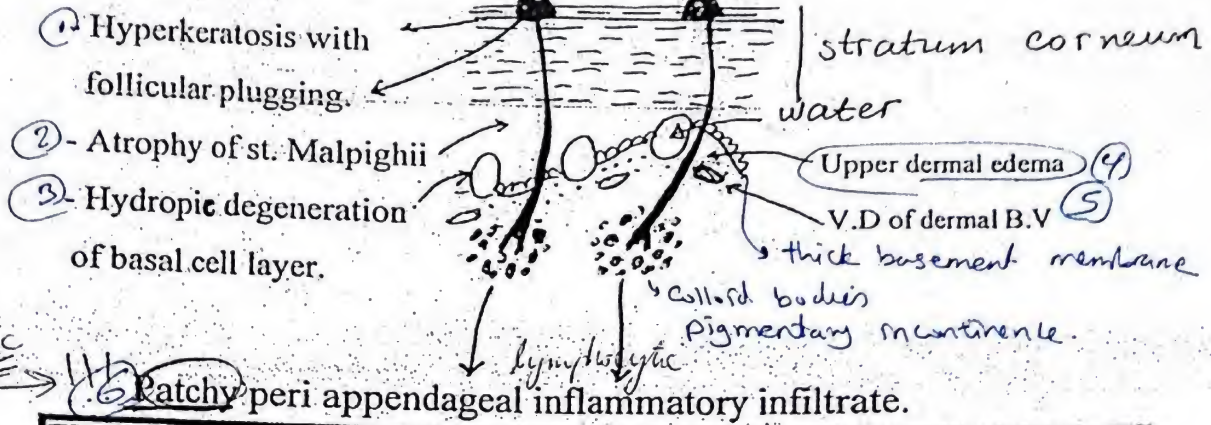
- Civatte bodies in Lichenoid tissue eruption
- Large apoptotic keratinocytes
- present as round or ovoid homogenous eosinophilic sm
- seen in dermatosis $\hat{=}$ degenerated keratinocytes
 \rightarrow (interface dermatitis)

as:- $\begin{matrix} \nearrow \text{LP} \\ \nearrow \text{FDE} \\ \nearrow \text{GVHD} \\ \nearrow \text{poikiloderma} \\ \nearrow \text{DLE} \end{matrix}$

*** Diagnosis :**

1. History & clinical examination.

2. Histopathology :



DD of patchy dermal infiltrate

1. LE.
2. Polymorphic light eruption.
3. Lymphocytoma cutis.
4. Lymphocytic infiltration of the skin (Jessner's)
5. Lymphocytic lymphoma.

Hydropic degeneration of basal cells :

- | | |
|---------------------|-----------------------------------|
| 1. LE. | 2. LP. |
| 3. Dermatomyocitis. | 4. Lichen sclerosis et atrophicus |

3. Immunofluorescence (lupus band test).

DIF : granular deposits of IgG at the dermo-epidermal junction (In 75% of active lesions)

4. Other lab examination :

- ↑ ESR.
- ↑ leucopenia.
- +ve ANA in very few patients.

-ve serology

① Systemic therapy for DLG:-

① Systemic antimalarial therapy (Gold standard):-

	Hydroxy-chlorquin	chlorquin	Quinacrine
safety	most safe	most toxic	
Dose	200-400 mg/d	125-250 mg/d	100 mg/d
eye	less toxic	more toxic	Not toxic turn skin yellow
max. dose	6.5 mg/kg B.w. most common used	3.5 mg/kg B.w	used in resistance to Hydroxy chlorquin

② Systemic therapy for antimalarial:-

- Dapsone 100 mg/d. For bullous eruption
- Retinoid
- Thalidomide
- steroid

- Differential diagnosis.

- Actinic keratosis.
- Seborrhic dermatitis.
- Plaque psoriasis.
- Polymorphic light eruption. } *hypersensitivity*
- Lichen planus.
- Lupus vulgaris → *scarring disease*

- Treatment:

① Topical

- ① Avoid sunlight.
- ② Topical sunscreen. *spf 15*
- ③ Topical steroid.
- ④ Intralesional injection of steroid

- ④ Topical calcineurin inhibitor
- ⑤ Topical retinoids

② Systemic treatment:

Skin pigmentation
Stop smoking
 Antimalarial: (Plaquenil)

- Dose: 200-400mg/day.

• Ophthalmogenic monitoring every 4-6w. (*Retinal detachment*)

- Systemic steroid for widespread or disfiguring lesions (should be limited to 4-6 weeks).
- Systemic etretinate 1mg/kgm BW may be indicated in hyperkeratotic DLE.

In case of failure of steroid/antimalarial therapy the following can be tried:

- Clofazamine (lamprane) 100-300mg/d.
- Vit. E 600IU/d.
- Dapsone 100mg/d (usually for bullous lesions).
- Thalidomide: highly effective but teratogenic & neurotoxic.

Powell's Syndrome:-

Erythema multiforme like + cut. LE

Diagnosis :- clinical

major criter

presence of LE (DLE, SLE, SLE)

LE-like lesion

Speckled pattern of ANA

minor criter

• anti Lc

anti Ra

• RF

3 major + 1 minor

Site :- Face, Neck, Chest

D.D → EM → pericardial by Hsu & RF & ANA & H by CsrH of cause

HIE → dermal edema, Keratinocyte Necrosis

DIF → at DEJ IgG, C3

* Chillblain → do serology to exclude LE

Chillblain

* variety of DLE go

go - ve serology

- Monoclonal CD4 antibodies is to be considered as a novel treatment for severe cutaneous LE.

Course & Prognosis :

1. 5% of cases may develop systemic LE.
2. 50% of cases with localized lesions → complete remission.
3. 10% of cases with generalized lesions → complete remission.
4. SCC & less commonly BCC → occur in the healed scar of DLE. (untreated lesion)

N.B. :

Chilblain LE :

- Is a chronic unremitting form of LE with acral distribution
i.e. : fingertip, rim of ears & heels, especially in women.
- It is usually preceded by DLE on the face.
- Pathogenesis : cold injury to the microvasculature.
- Treatment :

acral
♀
after DLE
cold
Trental

- Pentoxifylline. (red blood cell movement activator)
- The usual LE treatments are ineffective.

Trental →

neonatal LE
different varieties of SLE & antine

[III] Subacute Cutaneous LE (SCLE)

* Epidemiology :

- Age : Young or middle aged.
- Sex : female : male = 2 : 1.
- ↑ Incidence of HLAB8 - DR3.

* Clinically :

- Exacerbating factors : Sunlight.

- Symptoms :

→ Sudden onset of disfiguring erythematous eruption appearing on the upper trunk & dorsa of the hands.

→ +ve constitutional symptoms e.g. malaise ...

→ Photosensitivity.

- Signs :

→ Sites : Lesions usually affect the back, front of the trunk, around the neck, the arms (face is rarely affected).

→ Lesions are in the form of non-scarring psoriasiform papulosquamous (in 2/3 of cases) or annular polycyclic (in 1/3 of cases).

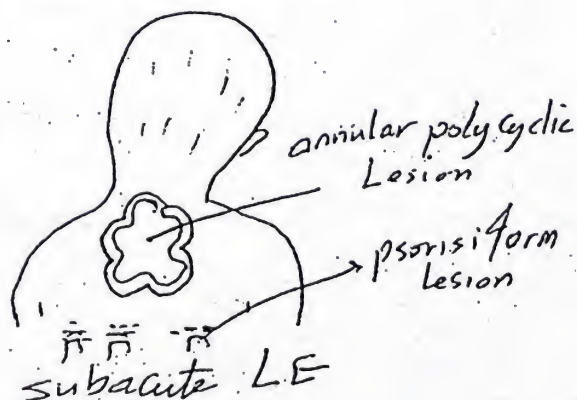
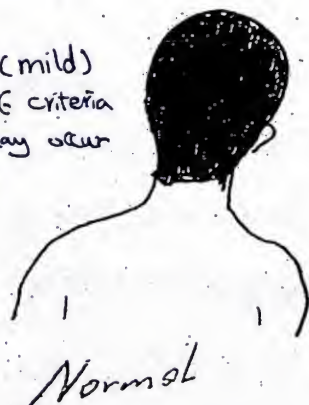
→ There is no scar or atrophy. → healed with greyish white hypopigmentation

→ Diffuse non scarring alopecia can be found.

LE → scarring
SCL → Not

★ Systemic lesion (mild)

- 50% Full fit SLE criteria
- Lung disease may occur
- Renal — rare

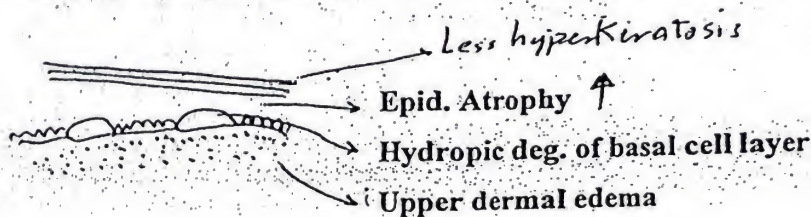


- Diagnosis :

→ History & clinical examinations.

→ Histopathology :

As DLE + more epidermal atrophy & less hyperkeratosis + prominent dermal edema & hydropic degeneration of basal cell layer.



→ Immunofluorescence : lupus band test --

DIF : +ve in 40% of cases.

→ Serological findings :

→ Low titers of ANA (homogenous pattern). Anti-Ab

anti - Ro +ve
anti - La +ve
↓ ANA

⇒ High levels of circulating immune complexes. IgG

⇒ Antibodies to RO/SS-A antigen are present in more than 60% & LA/SS-B much less commonly. (cytoplasm)

N.B. :

⇒ FANA → homogenous type in 60% patient

The extensive involvement is more seen in patient with chronic DLE.

Treatment :

1. Avoid exposure to heat & sun.
2. Avoid certain drugs e.g. Grisofulvin.
3. Topical corticosteroid.

4. Systemic therapy (the main-line of treatment)

a. Hydroxychloroquine 400mg/d for 4-8 weeks.

b. If the above failed retinoids (acitretin) may be tried.

teratogenic
c. Thalidomide (200-300mg/d) : very effective for skin lesions (but not for systemic involvement).

d. Dapsone & cyclosporin have been tried with varying results.

Prognosis & Course :

Very good, the skin lesions can completely disappear.

[III] Systemic LE

It is a serious multisystem disease involves the connective tissue & blood vessels.

*** Epidemiology :**

→ Age : 30y in female and around 40y in male.

→ Sex : female : male = 8 : 1 (more severe in black).

→ Family history +ve in 5% of cases.

*** Etiology :**

→ Genetic : more in pt with HLAB8 & DR3.

→ Heredity :

→ Drugs :

⇒ Flare up can be induced by contraceptive pills & hormone replacement therapy.

⇒ Hydralazine, anticonvulsants & methyldopa.

→ Viral agent.

→ Immunologic abnormalities : (there is loss of self tolerance)

⇒ B cell activation result in → hyper-gamaglobulinaemia.

→ UV radiation → important role in initiation disease.

o (Cytokines, Chemokines) → ↑ immune response

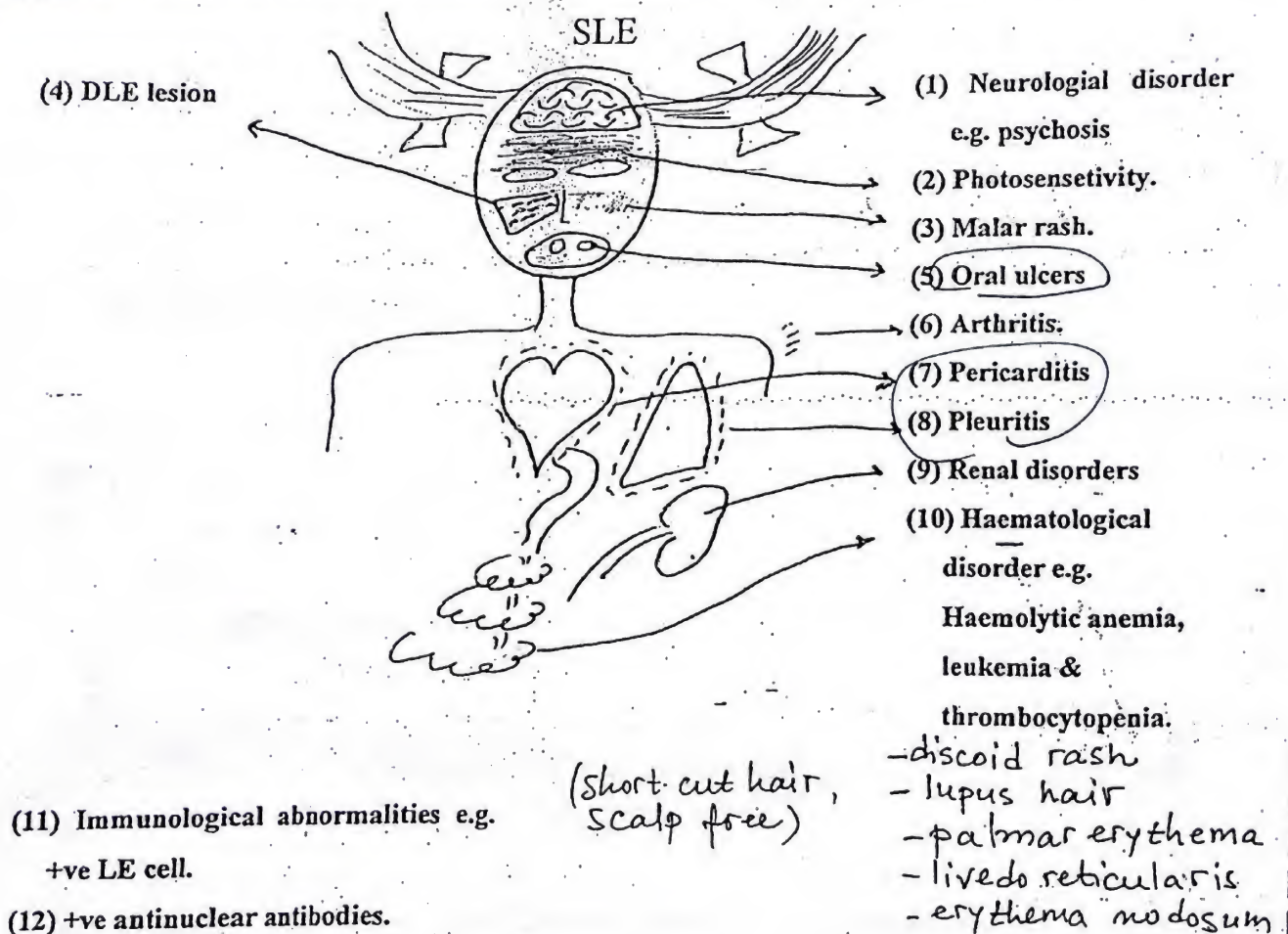
immunological → loss of self tolerance → B cell activation → ↑ Ig

⇒ Development of immune complexes from the circulation leads to → deposition of complexes in the tissue. Causing → vasculitis in different organs e.g. glomerulonephritis.

* Clinically:

- SLE is very variable in its manifestation.
- Mild cases may present only with arthralgia while severe cases may present with multisystem involvement.
- The duration of lesions is weeks (acute) or months.

1997 The American Rheumatism Association Criteria for diagnosis of



The presence of 4 or more of these criteria → diagnostic.

MD SOAP BRAIN

M → malar rash

D → Discoid LG

S → sensitisation pleuritis
pericarditis

O → oral ulcer

A → arthritides

P → photosensitive

B → haematological

R → Renal

A → ANA

I → immunological → the LG test ant-dsDNA
antism

N → neuropathy, psychosis

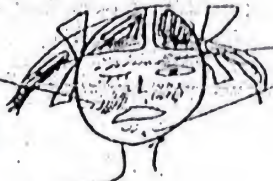
Cutaneous manifestations of SLE (+ve in 75% of cases)

(I) Specific lesions (diagnostic) :

(1) Malar rash heal

without scar

- on malar prominence
- spare nasolabial fold



(2) Photosensitivity :
dermatitis in
exposed areas.

(3) Bullus lesions : due to
separation at DEJ (may
be due to antibodies to
type VII antigen) best

treated by dapsone (MCQ)

Clinical → as BP, GBA

HIP → as OH, BP, GBA

② → bullous crusted lesion
as a result of intense
basal cell damage

③ dramatic acute eruption as TGV

(II) Non specific lesions : may occur

(4) wide spread erythema
on U shaped chest
shoulder
extensor of arm
back of hand

(1) Alopecia : (40-60%)

- Frontal with short broken off hair (lupus hair).
- Or diffuse non scarring.

(2) MM lesions erosion &
ulcers conjunctivitis &
gingivitis.

(3) Vascular lesions ^①periungual
telangiectases, ^②raynaud's
phenomenon,
lividoreticularis, palmar

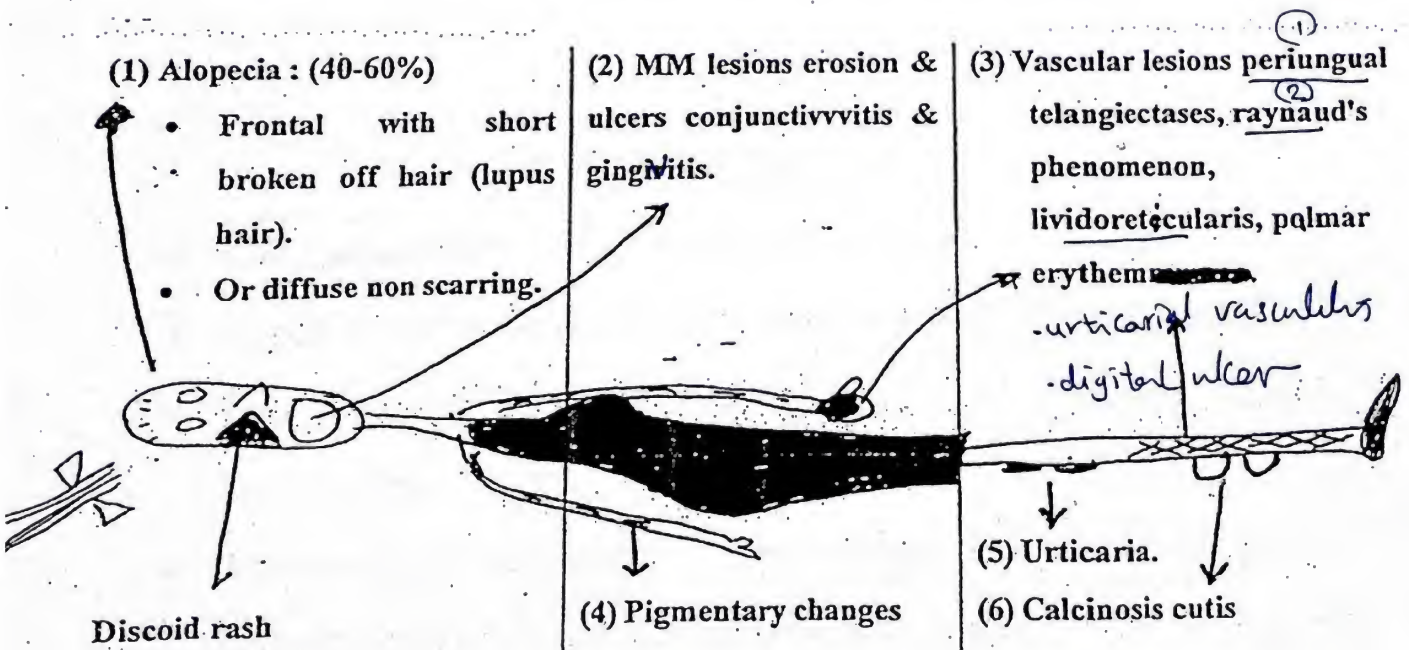
erythema
• urticarial vasculitis
• digital ulcer

(5) Urticaria.

(6) Calcinosis cutis

(4) Pigmentary changes

Discoid rash



Systemic manifestations of SLE :

(Renal) 20/05/05

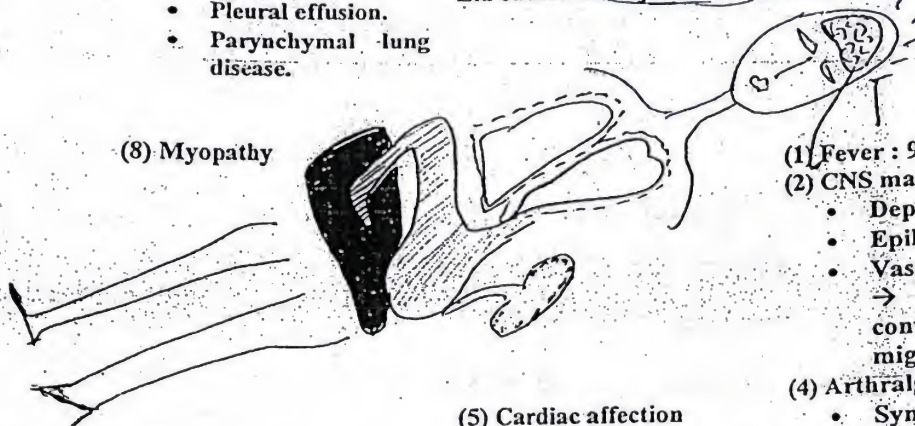
(9) Lung affection :

- Pleuritis.
- Pleural effusion.
- Parynchymal lung disease.

(3) Eyes :

* Retinal vasculitis. → retinal hge
Lid edema & conjunctivitis → in old patient, the anti Ro

(8) Myopathy



(1) Fever : 90% of cases.

(2) CNS manifestations :

- Depression.
- Epilepsy.
- Vasculitis of CNS
→ hemiplegia, convulsions & migraine ...

(4) Arthralgia : 90%

- Symptoms similar to rharthritis.
- Small joints commonly affected.
- Deformities uncommonly affected.
- Deformities uncommonly occur.

(5) Cardiac affection

- Pericarditis & pericardial effusion
- Myocarditis.
- Endocarditis.

(6) GIT affection

- Nausea vomiting & diarrhea.
- Oesophageal dysmatility.
- Ulcerative colitis.

Renal affection

- Clinical involvement occur in 40% of cases.
- Lupus nephritis is very important in assessing the prognosis.
- Focal or diffuse glomerulonephritis → chronic renal insufficiency → renal failure.
- The course is inconstant & albuminuria may persist for years without marked deterioration in renal function.

Associations :

- Rh arthritis, Hashimoto's thyroiditis, sjögren's syndrome & Dermatomyositis.

SLG { Focal mucoid degeneration.
Fibrin degeneration of CT
Liquefaction deg. of DEG
Fibrinoid degeneration of B.V.

Drug-induced lupus syndrome :

- Hydralazine – Isoniazid – D-penicillamine

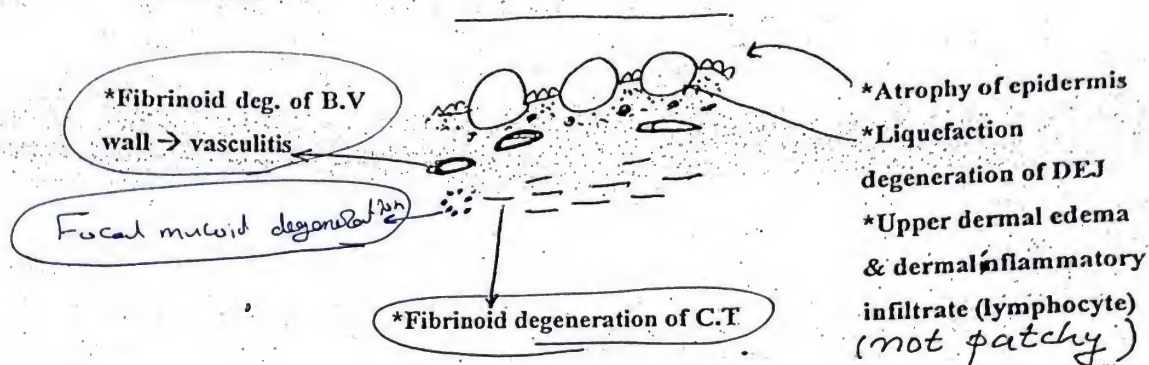
(to memorize them)

Diagnosis :

1. History & clinical examination

2. Histopathology :

a. Skin :



|||

b. Other organs : Widespread vasculitis affecting

capillaries, arterioles & venules → neurosis → systemic organ failure

3. Lab. Investigations :

⇒ Urine : proteinuria ($> 3.5\text{gm/d}$) cellular cast & RBCs.

⇒ Blood : pancytopenia.

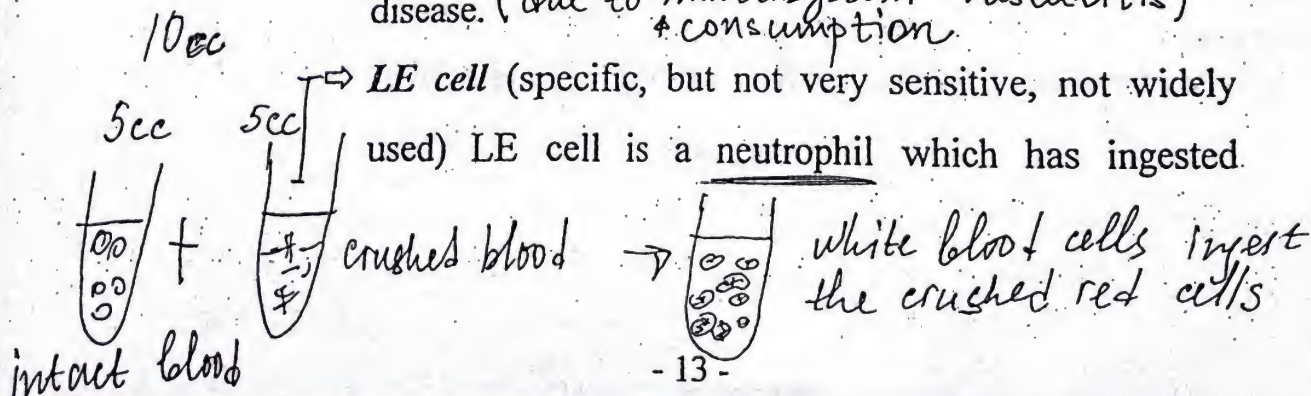
⇒ ESR : raised. (every month)

⇒ Wasserman reaction : +ve (nonspecific Ab)

⇒ Hypergammaglobulinemia : Rh. factor is +ve in 30-50% of patients.

⇒ Serum complement : levels are reduced during active disease. (due to multisystem vasculitis) + consumption

⇒ LE cell (specific, but not very sensitive, not widely used) LE cell is a neutrophil which has ingested.



basophilic homogenous nuclear material from another leucocyte in the presence of LE factor.

⇒ *Direct IF test (lupus band test)* :

- Detection of IgG & complement at DEJ (in sublamina densa).
- It is used to differentiate between DLE & SLE.
- It has a prognostic value.

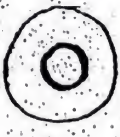



The test depends on detection of IgG & C in 3 areas :

1. Sun exposed diseased area.
2. Sun exposed uninvolved area.
3. Sun protected uninvolved area.

	DLE	SLE
(1) Sun exposed involved area.	+ve 90% cases	+ve in 90% of cases
(2) Sun exposed uninvolved area.	-ve	+ve in 78% of cases
(3) Sun protected uninvolved area	-ve	+ve in 55% of cases → indicate renal affection

⇒ *Indirect If Test (FANA test)* : (blood)

- +ve in 80% of cases.
- Using mouse liver as a substrate, 4 staining patterns can be demonstrated. + patient's blood + fluorescent material
- Diagnosis & prognosis differ accordingly to the type of FANA.

FANA	Antibody	Diagnosis	Prognosis
1) Peripheral 	n DNA →	SLE (specific) →	Poor
2) Homogenous 	n DNA → Nucleohistone →	SLE → SLE (drug induced) → not SLE	Poor Good
3) Nucleolar 	nuclear RNA	SLE Systemic scleroderma	poor
5) Centromere 4) Speckled  like broken glass	kinetochore Sm → RNP' →	CREST SLE (specific) → Mixed connective tissue disease →	Good Poor Good

⇒ **Serological markers**: (circulating Ab against Ag in nucleus and cytoplasm)

[I] Antibodies against nuclear constituents :

1) Anti DNA antibodies :

very 6 months) • Native DNA Abs = double stranded DNA Abs :

- Highly specific for SLE.
- Present in 70-75% of pt with active SLE associated with nephritis.
- Measured by RAI, ELISA or IIF.

• Single stranded DNA Abs :

- Present in 90% of SLE pt.
- Non specific (+ve in other C.T. diseases & occasionally in DLE).

Q Drug-induced LG: -

- hydralazine, procainamide, isoniazid.
 - produce LG like c/p
 - rare cut, Renal symptoms.
 - -ve anti-DNA
 - +ve ANA, +ve Anti histone.
 - improve w drug withdrawal

- D-penicillamine → differ in

- frequent cut, Renal c/p
- +ve anti-DNA

- Hydrochlorothiazides → SCLG-like lesion
+ve anti Ro

- Biologic inhibitor → +ve ANA, +ve anti dsDNA
No LE picture
-ve anti histone
DLG, sclE, photosensitivity → prominent

	Drug induced SLG	Drug induced sclE
skin	rare	sclE or gyrate erythema
sensitivity	Common	occasionally
Serology	anti-histone abs	anti Ro
Drugs	<ul style="list-style-type: none"> - hydralazine - D-penicillamine - minocycline - PUVA 	<ul style="list-style-type: none"> - thiazide - NSAIDs - antihistamine

2) Antibodies against small nuclear ribonuclear protein (S/RNP) :

• Anti-Sm antibody :

- Highly specific for SLE, but occur only in 25% of patients.
- Associated with high incidence of renal or CNS affection.
- Anti-nRNP (nuclear ribonucleoprotein) Abs +ve in mixed C.T disease.
- Anti La (SS-B) : +ve in 10% of patients with SLE

3) Histone antibodies :

- +ve in 30% of SLE.
- +ve in 90% of patients with drug induced SLE e.g hydralazine or isoniazide.
- C.P : rare cutaneous & renal manifestation.
- Serologically : anti DNA abs are absent.

N.B. : D. penicillamine - induced SLE differ in :

1. Frequent cutaneous & renal manifestations.
2. +ve anti nDNA abs.

[III] Anticytoplasmic Antibodies : (Ro, La)

- Small cytoplasmic ribonuclear protein (SC RNP) = Ro.

- Anti Ro abs is +ve in 25% of SLE pt's (To memorize)
- Anti Ro abs is also +ve in :

Ro → cytoplasmic glycoprotein

La → cytoplasmic RNA protein

ANA —ve SLE

- rare
- present $\hat{=}$ SLE
photosensitivity
anti Ro

anti Ro abs +ve in

- SLE
- Neonatal LG $\hat{=}$ $\hat{=}$
- late-onset LG $\hat{=}$ $\hat{=}$
- ANA —ve SLE
- Sjogren syndrome

ANA \longrightarrow more specific in SLE

anti dsDNA \longrightarrow specific, lupus nephritis monitor activity of nephritis

anti-sm \longrightarrow highly diagnostic, unique

anti-RNP \longrightarrow behaviour disturbance

anti Ro \longrightarrow SLE, NLE

anti La \longrightarrow usually $\hat{=}$ anti-Ro

RF \longrightarrow not-specific.

Drug-induced LG \longrightarrow according to drug.

anti Ro \longrightarrow hydroxychloroquine

anti dsDNA \longrightarrow biological

anti histone \longrightarrow hydralazine, SNA

ANA

-ve
exclude SLE
good -ve test

+ve
 \downarrow
R-specific
test
anti dsDNA
anti smDNA

ANA +ve in

healthy pregnancy
elderly
autoimmune, SS DM
Drugs
infection
neoplasia

To memorize

Anti Ro Ab
Extrinsically

- Subacute cutaneous LE, Neonatal LE, (40 days)
pleg & dryness
C2 deficiency LE, sjogren's syndrome,
late onset LE & ANA -ve SLE

⇒ Other investigation :

Brain CT or MRI

Treatment of SLE :

1. General measures : Rest & avoid sun exposure.
2. NSAID.
3. Prednisone 60mg/d in the following cases ~ 12th / daily 60-120mg
 - a. CNS involvement
 - b. Renal involvement.
 - c. Severly ill patients.
 - d. Hemolytic crisis.
4. Immunosuppressive drugs (Azathioprine or cyclophosphamide).
Imuran.
5. Antimalarial (chloroquine sulphate).
6. Lupus nephritis :
 - a. Higher doses of steroid + cyclophosphamide.
 - b. Renal dialysis.
7. Raynaud's phenomenon :
 - a. Vasodilators.
 - b. Avoid smoking & cold.
8. Plasmapheresis.

synthetic
immunosuppression

تحت المراقبة

SLE with Pregnancy

1. Deterioration of renal function occur in 10% of patients. ↑ *lupus nephritis*
2. Increase risk of premature delivery & perinatal mortality.
3. Risk is higher in female patients with +ve anti Ro abs or lupus anticoagulant abs.
 - pregnancy has no effect on SLE
 - therapeutic abortion not indicated
 - ↑ risk of IUFD in patient & the anticardiolipin Ab

➤ Contraception :

- Avoid contraceptive pills (aggravate the disease).
- IUD : high risk of hge & infection. *Contraceptive pills*
- Barrier methods one safest for patients. *steroids*

➤ Treatment :

- Systemic steroid.
- Asprin in low doses e.g. history of thrombosis.
- Closer fetal flow up.

Neonatal LE → type of SLE

- Female infants of mother who have or will develop C.T disease. → ↑ prevalence of HLA B3, DR3 of mother.
- The infant develop :

- Subacute CLE – like lesions (annular polycyclic scaly

erythematous lesions) mainly on the head & neck. It

develop within the first few weeks of life & improve spontaneously in 4-6 months, healing with no scarring.

- Photosensitivity can be prominent.

- Transient thrombocytopenia & low grade hepatitis.

- +ve Anti ro-abs in infant & the mother → disappear by 6 months of infant age

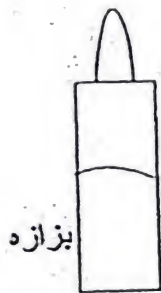
(site)

① Face → periorbital
lower eye
eye mask
not an eye

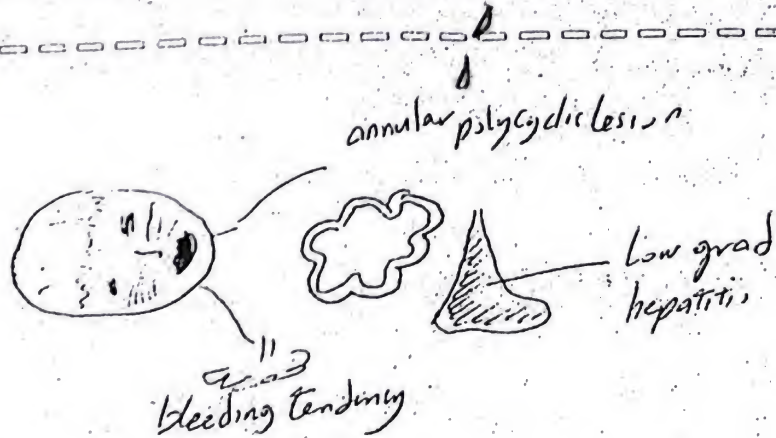
② scalp

③ extremities

not in mother



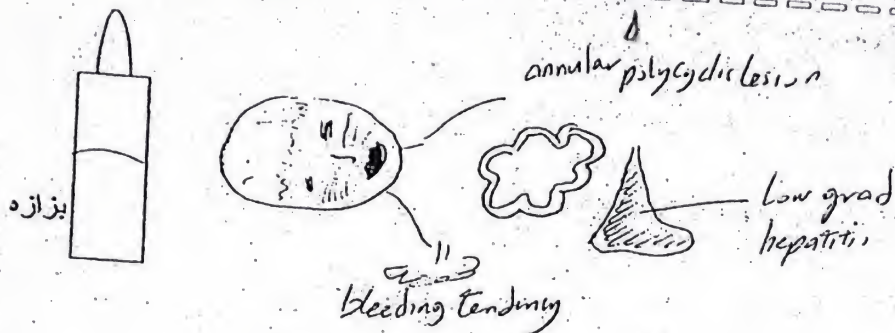
بازده



Late onset LE

- In the elderly (>50 years) characterized by :
 - ↑ incidence of neurological & pul. Manifestations.
 - Photosensitivity
 - +ve Anti -Ro-abs

مواجهه با آنزیم



Late onset LE

- In the elderly (>50 years) characterized by :
 - ↑ incidence of neurological & pul. Manifestations.
 - Photosensitivity
 - +ve Anti -Ro-abs

مظاهر

Neonatal LE

Q: Neonatal L.E.

- * it occurs Mainly in Female infants of Mothers who have or will develop Connective tissue disease.
- * ↑ prevalence of JLA-B8, DR3 in Mothers of Neonates with Neonatal LE.
- * Anti-Ro antibodies (Serological Markers) are present in both The Mother & infants, and disappear by 4-6 months of age from infant
- * Clinically:- The infant will develop:-

Cutaneous Manifestations

- (1) Subacute CLE-like Lesions in the form of "Scaly annular polycyclic erythematous lesions. That develop within the 1st 2 months of life. & improve in 4-6 months ;

Site :- (1) Face :- periorbital (raccoon eye)
(owl-eye)
(eye-mask)

- (2) Scalp
- (3) extremities.

Healing lesions resolve without scarring.

- (2) Photosensitivity (very common).

Extra-cutaneous Manifestations

- (1) Complete Congenital Heart disease block (Permanent) & may occur in absence of skin lesions.
 - (2) Hepatobiliary disease
 - (3) Transient Thrombocytopenia
- Both may be present at birth & develop with treatment.

Investigations

Infant should be evaluated for internal involvement:-

- (1) Cardiac (electrocardiogram)
 - (2) Hematological (CBC)
 - (3) Hepatic (Liver Functions test)
- When indicated

Treatment:-

- (1) Cutaneous lesions → Mild, require no treatment (Sun avoidance low potent Topical steroids)
- (2) Cardiac :- pacemaker always required.
- (3) hepatic & hematological → reversible (Self-limited)

Anti-phospholipid Syndrome

Definition: Anti-phospholipid Syndrome → Multiple System disorder characterized by:

- elevated APLs
- arterial / venous Thrombosis
- Thrombocytopenia
- recurrent spontaneous abortion.

(APAs) → heterogeneous group of circulating autoantibodies directed against:
- i.e. negatively charged phospholipid compound

→ include :: a) Anti-Cardiolipin

b) Lupus-anti-coagulant.

c) Anti β_2 glycoprotein I antibodies

These antibodies not bind to phospholipids themselves but bind to proteins bound to phospholipid, e.g. cardiolipin.

on 3 or more occasions at least 12 weeks apart

Types

(1) Primary APL antibody Syndrome

(2) Secondary APL antibody Syndrome

→ associated with Lupus, lupus like Syndromes, other diseases

Pathogenesis

The Mechanism of Thrombosis is not yet defined

May be:

① Activation of platelets → by interaction with platelet Membrane phospholipid → activation of coagulation

② Interference with anti-Thrombotic Mechanisms eg

- protein S and C pathways & anti-Thrombin III activity
- Release of endothelial prostacyclin / plasminogen activator
- Activation of prekallikrein → kallikrein

Clinical Features:

Cutaneous Manifestations

Q: Cutaneous Manifestations of Anti-phospholipid Syndrome.

Systemic affection

Many organ systems involved.

- ← (1) Deep venous Thrombosis (DVT)
- (2) Pulmonary embolism
- (3) CNS diseases.

- Arterial occlusion → brain ischemia repeated ischemic attacks.

(4) repeated Spontaneous abortion.

Catastrophic anti-phospholipid Syndrome

Multi-organ Failure (renal involvement Acute resp. distress syndrome)

precipitated by → (1) Surgical procedure

(2) infection

(3) discontinuation of anti-Coagulant Therapy

(4) Drugs (Captopril - Oral Contraceptive pills)

- 1- Pseudo reticularis
- 2- Ulceration
- 3- Necrosis

4- Raynaud's phenomena.

5- Acrocyanosis

6- Digital ischemia/gangrene.

7- Blue toe.

8- Purpuric / necrotic macules

9- Nodules

10- Thrombophlebitis

1- Hemorrhage

2- splinter hemorrhage

3- Porcelain white atrophic scar

Diagnostic Criteria: Diagnosis requires at least ① Clinical & ① Laboratory criterion.

Clinical Criteria

Vascular Thrombosis

more clinical episode of arterial / venous / or small vessel Thrombosis

Complications of pregnancy

or more → unexplained death → of Morphologically Normal fetus → at or after 10 wks of pregnancy

or more → Premature birth → of Morphologically Normal fetus → at or after 34 wks of gestation.

or more → unexplained → consecutive Spontaneous → before 10 wks of pregnancy abortion.

Laboratory Criteria

① Anti-Cardiolipin (IgM-IgG), Moderate or high titer

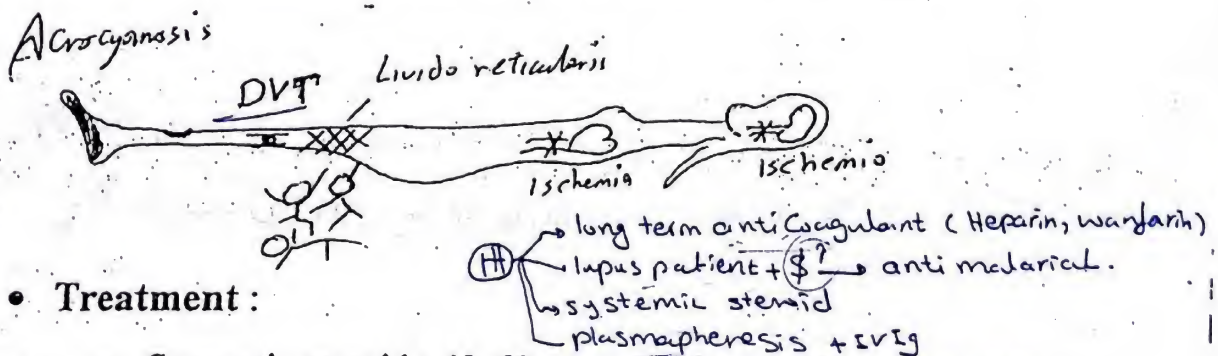
② Lupus anticoagulant Abs

③ β_2 glycoprotein I antibodies (IgM, IgG) > 99%.

on 2 or more occasions at least 12 weeks apart.

Antiphospholipid antibody Syndrome

- It is a hypercoagulable condition that leads to both venous & arterial occlusions.
- The main serological marker is the detection of circulating antibodies directed against phospholipid (Antiphospholipid antibodies).
Cell wall
- Antiphospholipid antibodies present in the form of lupus anticoagulant or anticardiolipin antibodies.
- Antiphospholipid antibodies have been detected by ELISA in 20-50% of cases of SLE & other C.T diseases. Behcet-syndrome, lymphoma, \$ & AIDS. not specific Ab
- **Clinically :**
 - Venous occlusion → DVT or axillary vein thrombosis.
 - Arterial occlusion → brain ischaemia or transient ischemic attacks.
 - Repeated spontaneous abortions.
 - Other features of the syndrome e.g. livedo reticularis. Acrocyanosis, Leg ulcers & thrombocytopenia.



• **Treatment :**

- Systemic steroid : 40-60mg prednisone + (in 2y disease)
- Asprin 75mg/d. Usually result in successful pregnancy.

N.B. : All women with SLE & repeated abortion should be screened for the lupus anticoagulant.

lupus anticoagulant antibody

Mixed Connective Tissue Disease (MCTD) Management of MCTD

Def: MCTD refers to

- ① Combination of features similar to those of SLE, SS, DM/PM and/or RA
- ② associated with autoantibodies to U₁-RNP

Overlap Syndrome → Two or more autoimmune disease occur in the same individual simultaneously
eg. SLE, SS, DM/PM, RA in various combination

Epidemiology: Age :: all age groups
Sex :: female: male 16:1

pathogenesis (pathophysiology of MCTD) ← Genetic, Immune, Inflamm

Genetic Susceptibility

HLA-DR₂, HLA-DR₄

Immunological dysregulation

• There is Both T and B cell response with less immune complex formation.

① B cell response :: ↑ high titre of anti U₁-RNP

② T cell response :: reactive T cells are found in peripheral blood.

③ Immune Complexes :: relatively low level of immune complexes found in the circulation (Compared to SLE)

Inflammatory response

• proliferative Vasculopathy in large, medium and small vessels with less inflammatory infiltrate.

• ++ Synthesis of Type III Collagen → result in abnormal Type I - Type III ratio.

Clinical Features: (Cutaneous Manifestations of MCTD) (Major diagnostic Criteria of MCTD)

→ Most, if not all, of the major organ systems may be involved during the course of MCTD.

① Fever.

② Skin & mucose membrane :: Raynaud's phenomena (75% - 100%) ← Most common skin change
• Malar rash, generalized erythematous rash, pigmentation / depigmentation.

③ Vascular involvement. Raynaud's phenomena

④ Muscles :: Myalgia - Myositis (in 30-50% of patients) → Similar to DM/PM.

⑤ Joints :: arthritis with deformities (in 60% of patients) → Similar to RA.

⑥ GIT :: Disordered Motility in upper GIT ← Commonest problem.

→ Symptoms vary from heart burn, Malabsorption, dysphagia, diarrhea.

⑦ Heart → All three layers may be involved, Pericarditis ← Commonest manifest. of cardiac involvement.

⑧ Lung → Major cause of death in MCTD is pulmonary hypertension

→ pleuro-pulmonary involvement → pleural effusion, pleuritic pain, PPH, Aspiration pneumonia, ILD

⑨ Kidney XXXX → absence of severe renal disease is Hallmark of MCTD.

⑩ Neurological involvement → XXXX Lack of CNS involvement.

→ Neurological manifest 20% of patients → PPT, aseptic meningitis.

Diagnostic Criteria

① Serological Criteria

Anti U₁-RNP → B cell at hemagglutination
≥ 1:1600

② Clinical Criteria

- (1) Raynaud's phenomena.
- (2) Swollen Hands (Edema)
- (3) Atherosclerosis.
- (4) Synovitis
- (5) Myositis

→ MCTD is present if:

① is associated with ③ or more Clinical criteria (one of them is Synovitis/Myositis)

Q. Symptom of MCTD.

- Symptoms
- ① Anti-U, RNP antibodies // highly characteristic feature of MCTD
 - ② ANA +ve
 - ③ RF +ve
 - ④ APL Abs occur less common than in those with SLE
 - ⑤ Absence of XXX anti-Sm Abs (differentiating MCTD from SLE)
anti-dsDNA
- Others
- Hypergammaglobulinemia
 - ⑥ - ↑ ESR
 - +ve Coombs' test
 - Anaemia / Leucopenia
- factor in patients, high titre, Coarse Speckled pattern
- 50 - 70% of patients.

* Management of MCTD:- (Management of MCTD).

→ According to the System(s) affected: for example:-

- * ① Mild MCTD → Raynauds ph. Arthritis, Fever
- avoid Cold exposure
 - NSAIDs
 - Low-dose steroids
 - Anti-malarial.

- ② Disease activity like RA
- NSAID
 - Low-dose steroids
 - anti-malarial.
 - Methotrexate or Immuno-suppressive drugs.

- ③ SLE-like (Mild-Moderate) involvement
- avoid Sun exposure.
 - Topical steroid.
 - Low dose steroid
 - anti-malarial.
- Severe organ involvement → Moderate to high dose steroids.
Cyclophosphamide
Other immuno-suppressive agents

- ④ Esophageal involvement without upper sphincter involvement
- Raise head end of the bed.
 - avoid coffee, Smoking.
 - Proton-pump inhibitors. (H₁)

- PAH (pulmonary arterial hypertension)
- asymptomatic → CCB, ACE inhibitors, UD
 - Severe → CCB, ACE inhibitors, Corticosteroids immuno-suppressive

A/e of DM:-

- unknown

- believed to be immune mediated response triggered by exogenous

① Genetic susceptibility:- HLA B8, DR2, DR52

② exogenous :- infectious → enterovirus

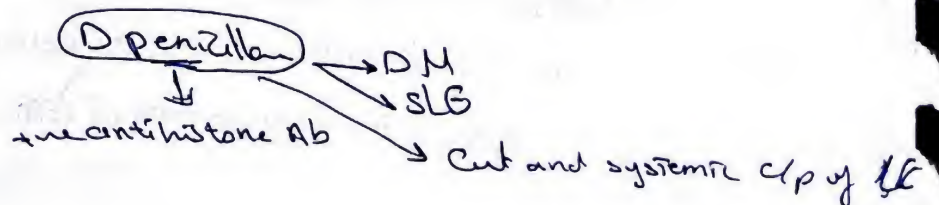
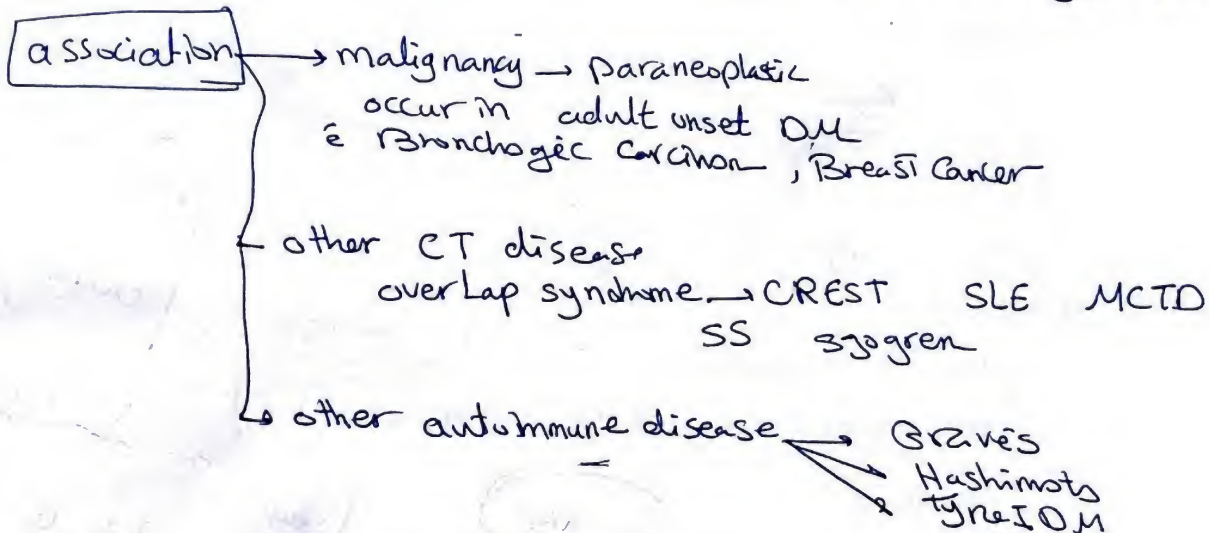
Drugs → D. penicillamine

malignancy → in adult onset DM

③ Immune response:- associated w/ other autoimmune disease

- presence of autoantibodies → ANA not specific

anti ku ← anti Jo1 anti Mi-2



34-1 and 2nd internal malignancy ✓✓✓✓

Dermatomyositis (DM)

It is a systemic autoimmune, inflammatory C.T disease affecting both the skin and muscles.

* Epidemiology :

- Age : ↑ 40y juvenile form of DM occur before the age of 10 years
- Sex : female : male = 2 : 1

* Classification :

- Polymyositis (PM)
- Dermatomyositis (DM)
- PM or DM
- Childhood DM.

* Etiology :

- Unknown.
- Int. malignancy e.g breast cancer, bronchogenic carcinoma..
- Autoimmune : several myositis-associated antibodies have

- Anti - Jo-1 abs : mostly seen in PM
- Anti - Mi-2 abs : in 20% of pt's with DM.
- Anti - Ku abs : marker for sclerodermatomyositis.

* Clinically :

Q (I) Cutaneous features : are often pruritus → d.d. of LG → not pruritus

1. Periorbital heliotrope violaceous erythema usually associated with some degree of edema of eyelids.


2. Gotttron's papule :


Flat topped, violaceous papules over the dorsal surface of interphalangeal joints of the hands.

3. Gotttron's sign :

Violaceous erythema overlying the dorsal aspect of hands.

4. Periungual erythema & telangiectasia + ragged cuticle. (Somite sign) not specific

5. Poikiloderma. \Rightarrow  mottling hypohyperpigmentation
red \rightarrow in LE \rightarrow shower sign \rightarrow distribution of poikiloderma on shoulder, arm, back

6. Calcinosis cutis: \rightarrow  slight up

Calcification in S.C tissues \rightarrow more in juvenile DM

7. Photosensitivity, Urticaria, hyperpigmentation in later stage & erythema multiform like lesions, acquired ichthyosis

(II) Skeletal muscle affection: (gradually, progressive)

- Progressive symmetric weakness & later atrophy of the proximal muscles of the extremities \rightarrow difficulty in rising from sitting without using arms.
- Muscle atrophy & muscle tenderness may be evident on palpation.
- Dysphagia is seen in 50% of patients due to esophageal muscle involvement. (esophageal dysmotility) he can not swallow without drinking water
- Involvement of the diaphragm may induce respiratory failure.
- myocytis \rightarrow progressive muscle weakness

Cpk \parallel creatine phosphokinase. (lab)
ischemic pain

⊕ Cardiac affection \rightarrow arrhythmia, myocarditis \rightarrow bad prognostic sign.

(III) Systemic manifestation: Rare in contrast to SLE malaise

N.B.:

- Pregnancy exacerbates DM in 50% of cases with increased incidence of fetal loss. DM can start in pregnancy.

LE \rightarrow pregnancy have no role
No fetal loss except in the 1st trimester

* myopathy
- classic cut. manifestation of DM is out muscle affection

* sclerodermatomyositis

scleroderma
Limited to
Face, hands

DM
or
PM

Raynaud's
non erosive arthritis
esophageal, lung affect

+ve RF
+ve DM-SCL Abs

* anti-synthase syndrome

- anti synthase Ab +ve
- anti Jo-1 +ve

Ray-
non erosive arthritis
interstitial lung disease
mechanic hand

Power

Diagnosis of DM:-

Up a few more to a few

- Biopsy → ~~not~~ poikilodermic site → LE-like H/P
Guthrie papule → acanthosis + Lichenoid infiltrate
- serum → ESR ↑ creatine phosphokinase ↑ LDH ↑ lactate dehydrogenase
ANA Anti Jo1 anti Mi2

• urine → creatine

— disease — disease — disease —

EMG electromyography → abnormal > 90% in DM

muscle biopsy → atrophy, necrosis, lymphocyte infi.
Not from deltoid that affected very late
From triceps muscle
done in case of absence of classic cut. lesion

Muscle imaging → Diagnosis

Diagnostic criteria For DM/PM:-

1. proximal symmetric progressive muscle weakness
2. Electromyogram of myopathy
3. Muscle biopsy → evidence of inflammatory myopathy.
4. Typical cut. lesion
5. elevated CPK, LDH, SGOT, SGPT

Possible
2 present

Probable
3 present

sure
4 present

○ ^{juvenile} Childhood DM, characterized by :

- Malignancy is rare.
- Much more severe than in adult.
- Calcification occurs more frequent + small vessel vasculitis
- Child recovers without any residual disability.
- Recurrences are rare.
- Low grade fever.

Diagnosis :

1. History and clinical examinations.

2. Laboratory investigations :

- (CPK)
- a. Creatine kinase : Elevated in acute active phase.
 - b. ESR : Elevated
 - c. Urine : Elevated urine creatin kinase.
 - d. Electromyography : Abnormal.
 - e. Muscle biopsy : Muscle atrophy a fibrosis.
 - f. +ve anti-Jo-1 antibody.

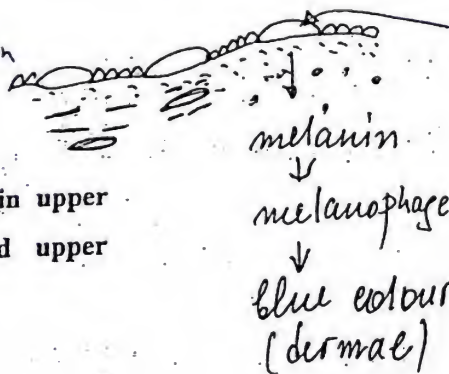
D.D of other
Causes of poikiloderm
- LG
- Psoriasis
- CTCL
- photo drug eruption

(III) Histopathology : LE

Skin :

mucin deposition

Fibrinoid deposits in upper dermis, and around upper dermal B.V.



Falttening of epidermis (atrophy)

Hydropic degeneration of basal cell layer

Upper dermal edema

Scattered inf. infiltrate

Muscle :

Muscle necrosis

* Treatment of Dermatomyositis :

* Management plan :: A patient with characteristic cutaneous eruption of DM should be submitted to:

- ① Skin biopsy :: to Confirm the diagnosis of DM.
- ② Search For Muscle disease (Myositis) → « affect Therapeutic decision »
- ③ Search For associated systemic disease → « affect Therapeutic decision »
- ④ Search For Feature of overlap with other AI CTDs.
- ⑤ Screening For Occult Malignancy (in adults with DM or amyopathic DM)
- ⑥ Start treatment accordingly

* Prognosis

* Indicators of good prognosis :: - Calcinosis cutis (Juvenile DM)
- Absence of Muscle affection (Skin-limited disease)

* Indicators of poor prognosis :: - Malignancy
- Cardiac disease
- pulmonary / GIT affection.
- Older age / progressive disease.
- Longer duration of Symptoms before diagnosis
- Extensive cutaneous involvement of The Trunk.
- Initiation of Therapy after 24 Months (2y) of Muscle weakness

* Causes of Death in DM :: - Malignancy
- Cardiac Failure.
- respiratory infection.
- Malnutrition (Difficulty in Swallowing)
- Side effect of Steroid Therapy.

* Treatment

Treatment of Cutaneous disease ::

- 1) Photoprotection (SunScreen)
- 2) Topical Corticosteroid / Tacrolimus.
- 3) Anti-malarial Therapy
- 4) Immuno-Suppressive :: Low dose weekly Methotrexate
Mycophenolate Mofetil.
Dapsone, Thalidomide.
- 5) IVIg
- 6) Retinoids
- 7) Biologic :: TNF- α blockers (infliximab - Etanercept)
Rituximab.

8) tt of Calcinosis cutis ::

- Surgical excision
- Calcium channel blockers (diltiazem).
- ESWL (electric shock wave lithotripsy)

Treatment of Muscle disease .

- (1) Rest (in acute stage).
- (2) physiotherapy (to prevent deformity & Contractures)
- (3) Systemic Corticosteroids
Prednisone 1mg/kg/day
- (4) Pulse Corticosteroid +
Steroid Sparing agents
(For Severe cases)

Methotrexate, Azathioprine, Mycophenolate
cyclophosphamide, cyclosporine, IVIg
Etanercept, infliximab, plasmapheresis.

* Wong's dermatomyositis *

- Rare DM Subtype
- Characterized by
PRP-like lesions
(Hyperkeratotic cutaneous lesions
that resemble clinically & histopathologically
PRP in DM patient)

Treatment :

1. Complete rest.
2. Prednisone 0.5-1 mg/kg BW/d increased to 1.5 mg/kg.
3. Azathioprine, cyclophosphamide or cyclosporine.
4. Methotrexate.
5. Antimalarial. *Plaquenil 200mg x 2*
6. High-dose of IV immunoglobulin bolus therapy/monthly.
7. Topical steroid & sunscreen (for photosensitivity).
8. Malignancy should be excluded.
Elidel (pimecrolimus)

(Mikulick's disease)

SJÖGREN'S Syndrome

Def / autoimmune disease affect → secretory gland

This syndrome comprises the triad of :

1. Dryness & atrophy of the conjunctiva and cornea.
2. Dry mouth.
3. Rheumatoid arthritis. *Morning stiffness*

Associated systemic features :

Cutaneous manifestations

- Arthralgia.
- Dysphagia.
- Raynaud's phenomenon
- Renal affection.

- xeroderma
- urticarial vasculitis
- petechiae
- erythema
- purpura

Treatment : Artificial tears + saliva replacement solutions. *+ immune suppressive in organ involvement*

Lab → ↑ ESR, leucopenia RF +ve anti Ro anti La

H&P → Dense lymphocytic infiltrate around salivary gland

Peri-ocular dermatitis
dermatitis

* Raynaud's phenomena

→ Def: Episodic Vasoospasm of The digital arteries (Secondary to cold stimuli) → White, blue, and red discoloration of The fingers.

→ 2 types: primary and secondary

Primary Raynaud's

- Synonyms
 - Raynaud's disease.
- Incidence
 - Common
- Association
 - Not associated with underlying disorder
- Age of onset
 - Puberty
- Sex
 - ♀:♂ (20:1)
- Frequency of attacks
 - < 5 per day
- precipitants
 - Cold
 - emotional stress

Secondary Raynaud's

- uncommon.
- associated with underlying disorder e.g (SSc is one of Common)
- > 25 yrs
- ♀:♂ (4:1).
- > 5-10 per day
- Cold.

- Ischemic injury
- Abnormal Capillaroscopy
- autoantibodies (AMA, Anti SCL-70, Anticentromere)

Absent

Present

→ Treatment:

1st Line → avoid Cold. & Tobacco products.

- 2nd Line →
- (1) \downarrow CO → CCB (nifedipine)
 - Ang II receptor blocker (Losartan).
 - PDE5 Type 5 inhibitor (sildenafil / tadalafil)
 - (2) \downarrow low dose aspirin, Pentoxifylline
 - (3) IV PGE1
 - (4) Nerve block, Sympathectomy.
 - (5) Topical Preparations (Ineffective)

* Eosinophilic Fascitis (Shulman's Syndrome)

→ Sclero-derma like Syndrome. , Deep Fascitis with eosinophilia.

3-10% of Trauma (30%)

(GP)

... (Initially) → Oedema & pain of involved extremities

↓
quickly progress to Fibrosis & dimpled appearance.

* Condition affect extremities, in Symmetric fashion.

* (Groove Sign) → Linear depressions where veins appear to been sunken within indurated skin.

(Lab) ↑ ESR - Hypogammaglobulinemia - peripheral eosinophilia

(Associated) → pancytopenia (Anaemia / Thrombocytopenia) + Hematologic Malignancy (Myeloproliferative disorder).

(H/P)

→ Dermal Fibrosis
Thickening of deep fascia (10-50 times The normal width)
patchy infiltrate (lymphocytes-plasma cells) in fascia

(Treatment)

* Prompt Treatment (oral Corticosteroids) → to preserve Mobility & Function

* if Inadequate → Methotrexate / cyclosporine
• Hydroxychloroquine.
• PUVA-UVA₁ } → used alone or Combined to prednisone

Handwritten signature

Scleroderma

It is a multisystem disease of unknown cause. It may be localized to the skin (morphea) or involve the skin and internal organs.

Scleroderma

Localized (morphea)

Systemic sclerosis



*Limited cutaneous
systemic sclerosis*

*Diffuse cutaneous
systemic sclerosis*

Limited CSS

Diffuse CSS

• Onset	Gradual	Abrupt
• Skin sclerosis	Face, forearm & hands.	Hands and Trunk
• Raynoud's phenomenon	<i>Raynoud's</i> Long history	Within one year of onset of skin changes
• Systemic affection	Late onset of pul. Hypertension	Early onset of lungs heart stomach & renal diseases
• Nail fold capillary	Dilatation	Dilatation & destruction
• Auto antibody	+ve anticentromer AB	+ve SCL 70 AB -ve anticentromere AB
• Prognosis	Good	Poor

Localized Scleroderma (Morphea)

* Definition :

It is a localized cutaneous sclerosis characterized by early violaceous, later ivory-white plaques, which may be solitary, linear, generalized & rarely accompanied by atrophy of underlying structures.

morphea is differentiated from systemic sclerosis by absence of sclerodactyly, Raynaud's phenomenon, nail fold capillary change, organ involvement

* Epidemiology :

Female : Male = 3 : 1

Age : 20 - 40 years.

* Etiology :

Unknown, it may be caused by *Borrelia burgdorferi* infection.

* Clinical varieties : systemic C/P — not rare most common arthralgia, CNS sclerosis

1) Plaque (circumscribed) morphea: most common presentation in adult

- Site : Trunk, Limbs, face & genitalia.

- C.P : Single or multiple plaques, indurated in consistency,

Ivory white in color with violaceous lilac border.

- head & residual pigmentation

2) Pansclerotic morphea (morphea profunda) :

- Site : there is involvement of dermis

fat, muscle and bone pansclerotic morphea

is usually generalized occurring on the trunk

extremities, face and scalp with sparing of

finger tip and toes.

3) Segmental morphea : (U/A 1)

- Site : Face.

- Hemiatrophy on one side of the face.

4) Guttate morphea :

- Site : Trunk.
- C.P. : Small whitish atrophic macules resembles lichen sclerosis et atrophicus but doesn't show hyperkeratosis or follicular pluggings.

5) Generalized morphea :

- It occurs initially on the trunk. Extensive involvement → restricted respiration.
- There is no systemic involvement.

- Bullus lesions may be seen !! (the only type of scleroderma)

6) Linear morphea : (en coup de sabre) lesion only

- Sites : most common presentation in children

* It usually occur on extremities → contracture of joints.

* Face : En coup de sabre : Linear depressed groove on the frontoparietal region, scalp involvement → alopecia.

* Nail dystrophy may occur.

7) Bullous morphea

8) as a component of overlap syndrome
MCTD scleroderma myositis

Diagnosis :

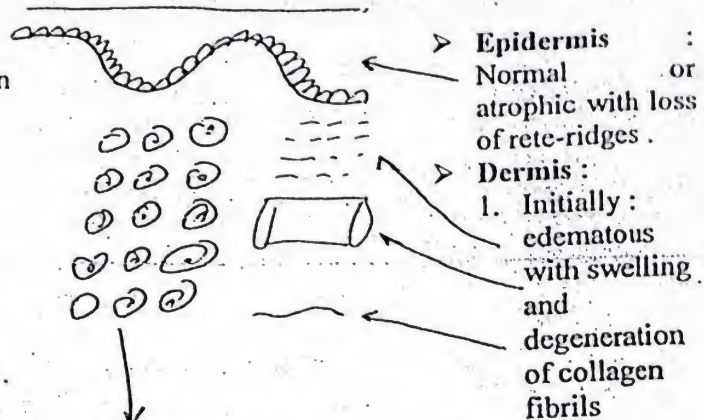
1. History & examination
2. Histopathology :

Early

(1) Edema
swelling degeneration
of collagen fibrils

early inflammatory stage:-

- lymphocytic inf. inf. in
Lower dermis, sc fat
- Large area are replaced by
newly formed collagen
- thick trabeculae of sc fat.
- ↑ mast cells



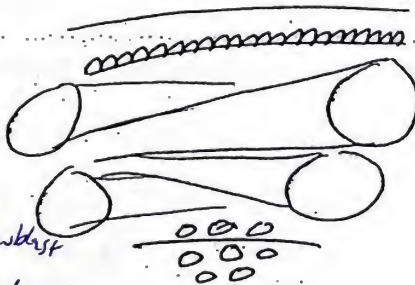
2. Slight inflammatory
infiltrate:

- Perivascular or
diffuse.
- lymphocyte, macrop-
hage or plasma cells.

Later

Late sclerotic:-

- infiltrate disappear.
- Collagen consist of
thick closely packed
hyalinized bundle & fibrils
- atrophic eccrine gland.



- > Epidermis: Atrophic
- > Dermis:
 - Thickened with few
fibroblast & dense
collagen.
 - Inflammatory cells at
dermal/subcutaneous
junction.

Treatment:

1. Intra lesional injection of triamcinolone.
2. Penicillamine (Antifibrotic agent).
3. PUVA.

Systemic Scleroderma (Systemic sclerosis)

more in 4th decade

♀ 4:3:1

Scleroderma is a multisystem disorder characterized by inflammatory, vascular and sclerotic changes of the skin and a variety of internal organs especially the lungs, heart and GIT.

* Etiology:

- Unknown.
- Autoimmune.
- Vascular changes.

مترشح به بافت سفت و سفت می شود

* Clinical features:

[I] Limited cutaneous systemic sclerosis:

acroscclerosis

CREST

- It starts with Raynaud's phenomenon many years before any skin changes.

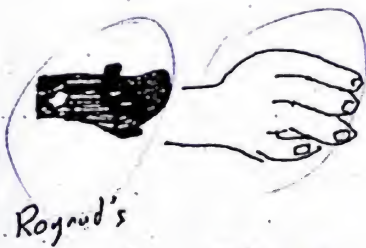
• Clinically:

A. Symptoms (A) Raynaud's phenomenon with digit pain, coldness & tingling.

B. Cutaneous examination:

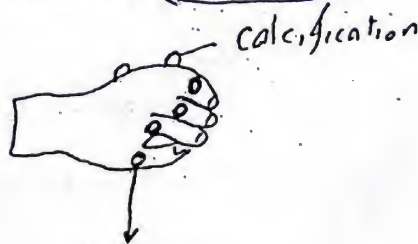
1. Hands and Feet:

- R ▪ Early Raynaud's phenomenon with color changes e.g. pallor, cyanosis & rubor.
- E ▪ Non-pitting edema of the ^{hands} & feet → can't be fully extended.
- U ▪ Painful ulcerations at fingertips & knuckles may occur
- C ▪ Cutaneous calcifications of fingers may be seen.
- T ▪ Periungual telangiectasia.

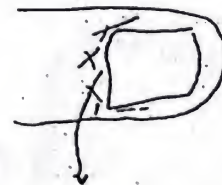


Raynaud's

Edema



Ulceration



periungual telangiectasia

• disseminated telangiectasia.

- Raynaud

1) Hand and feet

Raynaud

edema

ulceration

- calcification

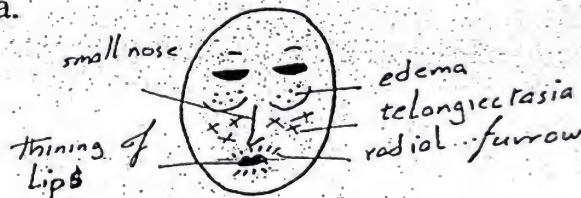
telangiectasia

2. Calcinosis cutis :

- Whitish papules occurs over bony prominences. It may ulcerate and extrude white paste.

3. Face :

- Early: Periorbital edema.
- Later : edema & fibrosis result in loss of normal facial lines, thinning of lips, microstomia, radial perioral furrowing & small sharp nose + fascial telangiectasia.



4. Hyper & hypopigmentation.

5. CREST syndrome : consist of

- Calcinosis.
- Raynaud's phenomenon.
- Esophageal dysmotility.
- Sclerodactyly.
- Telangiectasia.

C. Systemic manifestations :

Esophageal symptoms, pulmonary hypertension ...

[III] Diffuse cutaneous scleroderma (DCSS)

skin sclerosis involve acral
No telangiectasia.
short interval < 1 year b/w
between Raynaud and skin
changes

A. Symptoms :

- o Early involvement of organs → e.g. GIT → anorexia & weight loss, lung → dry cough ...

Diffuse

DCSS

A. Early involvement of organs → GIT involvement

B. Cutaneous examination :



○ Raynaud's phenomenon develop later (after 1 year).

○ Skin lesions :



▪ Hand changes start first. skin become edematous.

▪ There is telangiectasia and abnormal nailfold capillaries.



▪ Diffuse swelling & stiffness of fingers occur.

▪ Stiffness may involve most of the body in severe cases → later the skin becomes atrophic.



C. Systemic Manifestation :

○ Musculoskeletal manifestations :

▪ Pain & stiffness of fingers & knees.

▪ Polyarthritis ...

○ Gastrointestinal manifestations :

▪ Esophageal dysmotility, malabsorption.

○ Respiratory manifestations :

▪ Lung fibrosis.

○ Renal affection.

○ Heart affection.

○ CNS affection.

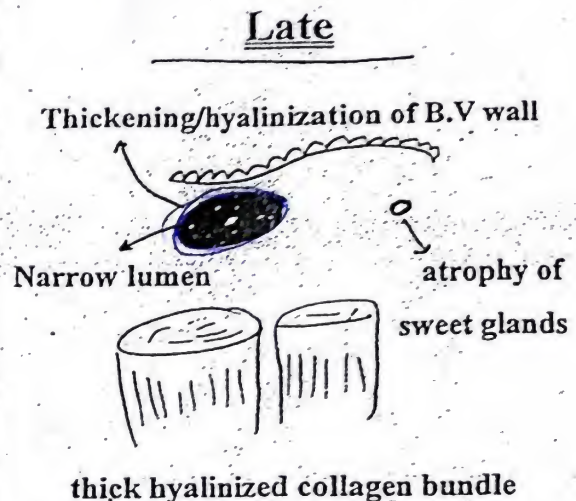
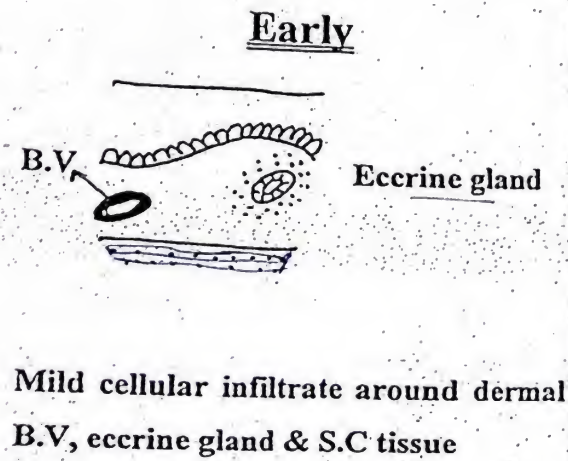
○ Eye affection.

N.B. : Sometimes systemic manifestations occur without skin involvement (scleroderma sine scleroderma)

Diagnosis :

1. History & examination.

2. Histopathology :



3. Lab. Findings :

- In localized CSS : +ve anticentromere antibody.
- In diffuse CSS : +ve SCL-70 antibody.
- Rheumatoid factor : +ve in 30% of cases.
- ESR : may be +ve.

[III] Radiography :

- Chest x-ray : honey comb lung
- Barium swallow – for impaired esophageal motility.

Diagnostic criteria (American College of Rheumatology)

in 91% certain with ① major or ② minor criteria

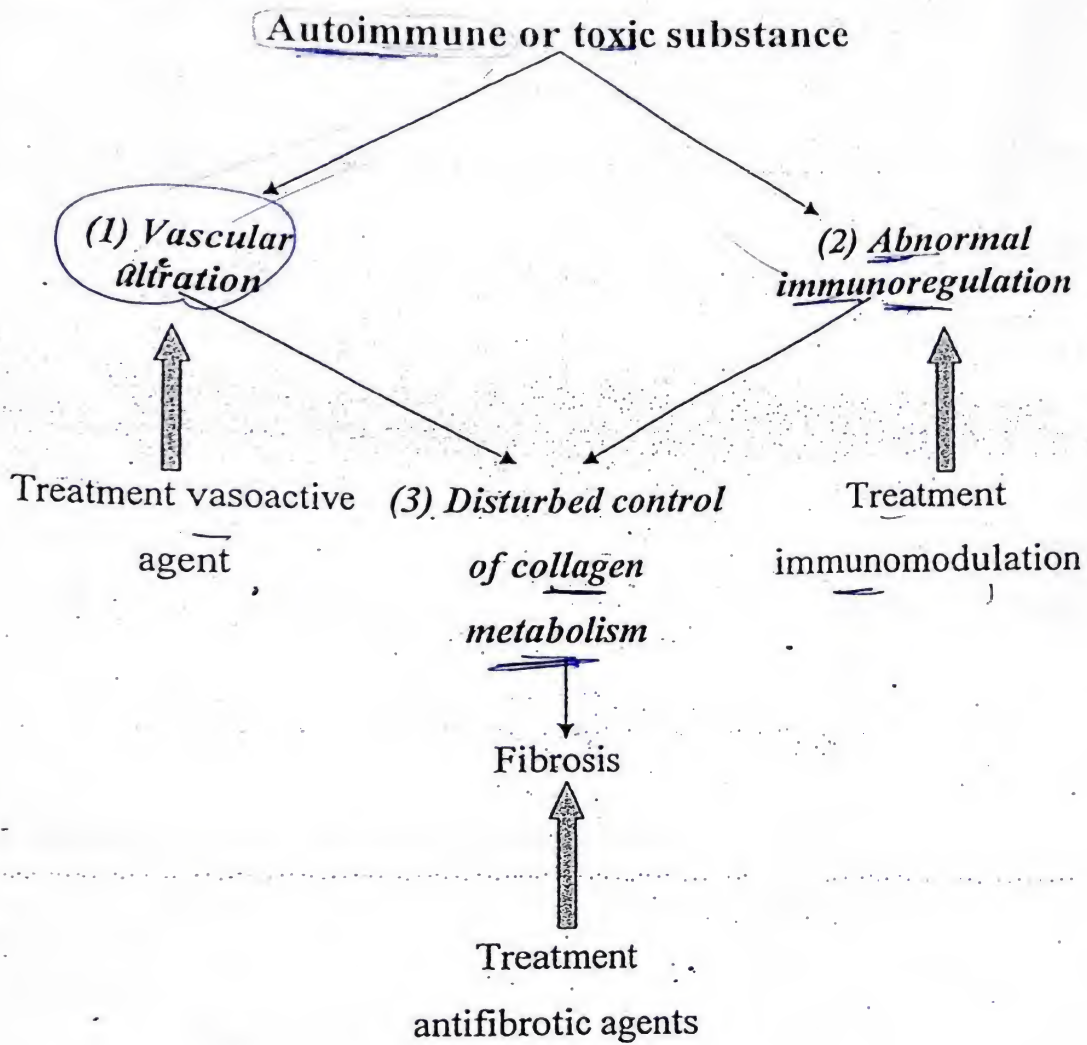
major

proximal (truncal) sclerosis

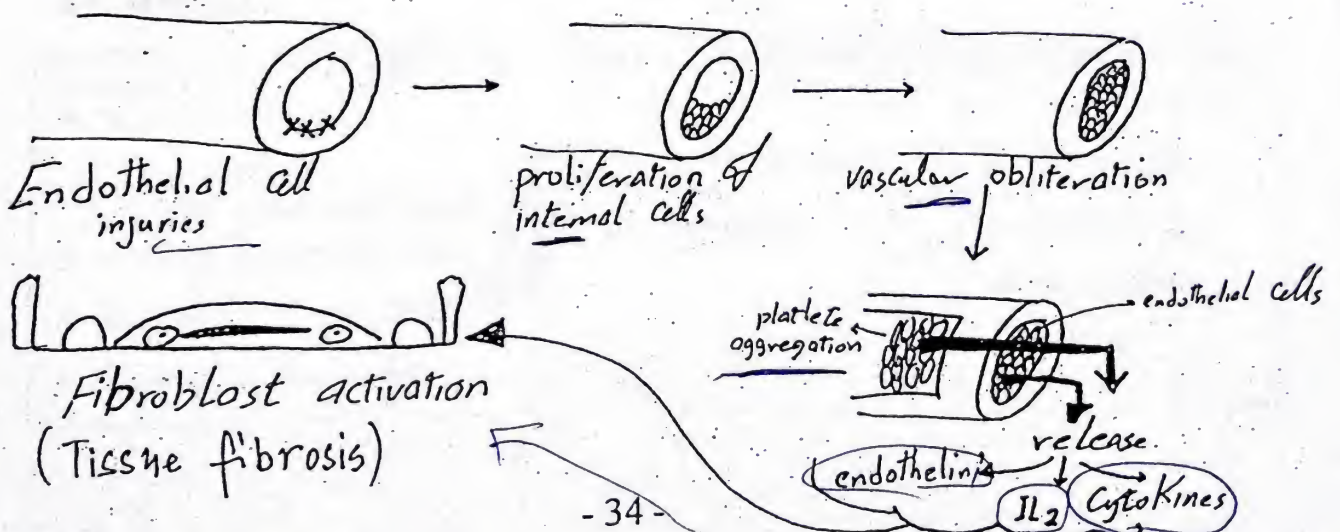
minor

- sclerodactyly
- digital pitting scar
- loss of substance of digit finger pad
- Bibasilar pulmonary fibrosis

Pathogenesis :



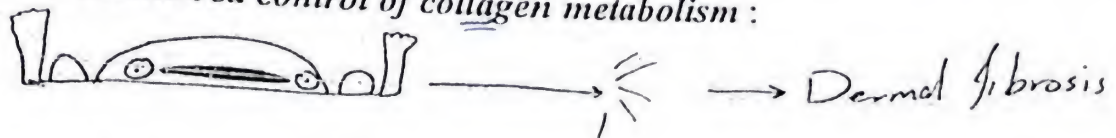
(1) Vascular alteration :



(2) Abnormal immunoregulation :

- Humoral immunity \rightarrow \uparrow antinuclear AB.
- \uparrow TH cell activity.

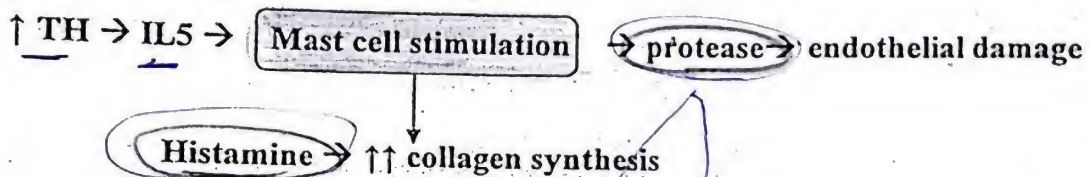
(3) Disturbed control of collagen metabolism :



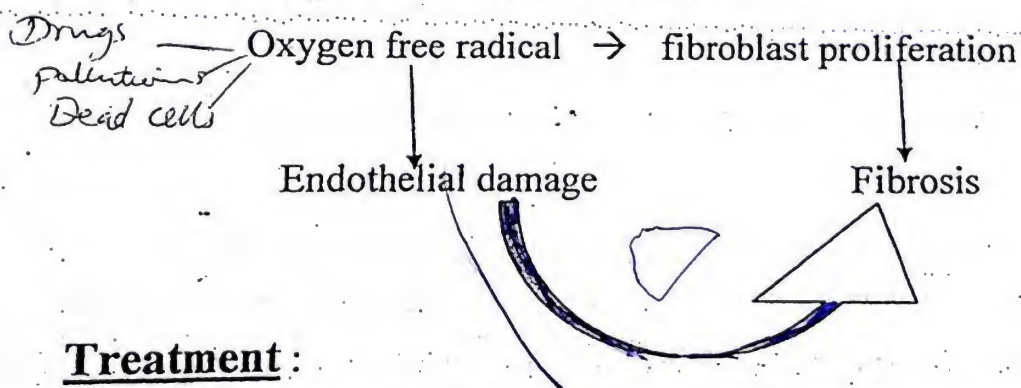
Activated fibroblast \rightarrow \uparrow synthesis of collagen type I & II +
fibrinectin + glycosaminoglycans \rightarrow lower dermal fibrosis
+ fibrosis in internal organs.

N.B. :

---* Role of mast cell in scleroderma :



* Role of oxygen free radical in scleroderma :



Treatment :

(1) Vaso-active agents	(2) Immunomodulators	(3) Antifibrotics
a. <u>Prostacyclin</u> : - Vasodilator. - Inhibit platelet aggregation b. Low M. weight dextran : c. <u>Nifedipine</u> : vasodilators. d. <u>Captopril</u> : vasodilators	a. <u>Prednisone</u> 5-10 mg/d b. <u>Cyclophosphamide</u> c. <u>Azathioprine</u>	a. <u>D.pencillamins</u> . b. <u>Colchicine</u> . c. <u>Isotretinoin</u> d. <u>Grisofulvin</u> e. <u>PUVA</u>

Pseudoscleroderma

Many diseases or environmental factors can induce sclerodermatous changes e.g.:

1. Genetic :

- Rothmund – Thomson syndrome.

- progeria

2. Metabolic :

- Amyloidosis.
- Porphyria cutanea tarda.
- Scleroderma.
- Scleromyxedema.

POEMS syndrome
polyneuropathy
organomegaly
endocrinopathy
OH
skin lesions
sclerodermatous
myxedema

3. Paraneoplastic syndromes :

- Carcinoid syndrome.
- Bronchogenic Carcinoma

4. Graft versus host disease. GVHD (chronic)

5. C.T. diseases :

- SLE.
- Dermatomyocitis.
- RA

6. Occupational :

- Silicosis.
- Vibration syndrome.

Eosinophilic fasciitis (shulman's syndrome) (type of plaque morph)

It is an inflammatory disorder characterized by subsequent induration of the skin & SC tissues associated with peripheral

eosinophilia.

Treatment :

1. Prednisone 40mg/d.
2. Methotrexate.
3. Cyclosporine A.

immune modulator

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